

REMARKS

A. Regarding the Amendments

Claims 67, 91, and 95 have been amended to claim the subject matter of the present invention with greater specificity and particularity. More specifically, with respect to claims 67 and 91, the limitation "ataxia" has been deleted from the Markush groups reciting various mitochondrial disorders. Consequently, the scope of claims 67 and 91 has been narrowed accordingly. With respect to claim 95, the dependency has been changed and the subject matter recited in claim 95 has been split between claim 95 and newly added claim 110. New claims 96-110 are dependent claims that depend, directly or indirectly, on the allowed claim 95. No new matter has been added either in the amendments to claims 67, 91, 95 or in the new claims.

The Applicant acknowledges the withdrawal of the previous rejections of claims 74, 76-79, 82 and 83, under 35 U.S.C. § 112, first paragraph (enablement). The Applicant also points out that according to the cover page of the Office Action claim 74 has been rejected. However, the Office Action itself is silent with respect to claim 74 and provides no reason or explanation for the rejection. The Applicant respectfully requests clarification. Upon entry of this amendment, claims 67, 70, 73-81, 84-91, and 95-110 will be under consideration.

B. Rejections Under 35 U.S.C. § 103 (a)

Claims 67, 70, 73, 75-78, 80, 85, 89-91, and 93 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Naviaux et al., "Mitochondrial Dysfunction in Human Pathology," Melbourne, Australia, September 7, 1998 (page 2, lines 20-22 of the Office Action). This rejection is respectfully traversed. Furthermore, claims 67, 70, 73, 75-81, 84-91, and 93 also stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Page et al., "Developmental Disorder Associated with Increased Cellular

Nucleotidase Activity," *Proc. Natl. Acad. Sci. USA*, vol. 94, pp. 11601-11606 (1997)
1998 (page 3, lines 17-18 of the Office Action).

The standard that has to be satisfied for making a *prima facie* case of obviousness has been provided in the response to a previous Office Action, filed December 12, 2005. The Applicant submits that the criteria of this standard have not been met, either in view of the Naviaux et al. reference or the Page et al. reference.

More specifically, turning now to the Naviaux et al. paper, this reference does not qualify as a prior art reference. Indeed, the effective filing date of the present application is February 23, 1999, which is the filing date of the provisional application USSN 60/121,588, to which the present application claims priority. The publication date of the Naviaux et al. reference is September 7, 1998, i.e., less than one year prior to the effective filing date of the present application. Accordingly, the only possible way the reference may be used for the obviousness rejection is under 35 U.S.C. § 102(a)/103(a).

The Applicant respectfully reminds that on March 9, 2005, the Applicant filed a Declaration under 37 C.F.R. § 1.131. In the subsequent mailed June 6, 2005, the Examiner agreed (page 2, line 20 through page 3, line 4) that the Declaration properly antedates U.S. Patent No. 6,472,378 to von Borstel. Since the reference date of the von Borstel patent is August 31, 1998, which is seven days earlier than the publication date of the Naviaux et al. paper, antedating von Borstel will necessarily mean the Naviaux et al. reference is also automatically antedated.

Because the present rejection must be only under U.S.C. § 102(a)/103(a), antedating a reference via a 131 declaration is clearly proper. Accordingly, it is submitted that the Naviaux et al. paper is not a proper 103 reference and cannot be used to make a *prima facie* case of obviousness.

With respect to the Page et al. paper, the reference discloses treatment of various developmental disorders, but fails to disclose or suggest treatment of mitochondrial

disorders recited in claims 67 and 91. To cure this deficiency of Page et al., the Examiner had previously proposed to combine Page et al. and U.S. Patent No. 6,472,378 to von Borstel. However, as correctly recognized by the Examiner in the June 10, 2005 Office Action, in view of the above-mentioned 131 Declaration, von Borstel does not qualify as prior art under any sub-section of 35 U.S.C. § 102, and therefore cannot be used in combination with any other reference for making a *prima facie* case of obviousness.

Accordingly, the Examiner has stated that von Borstel is not even needed for making a *prima facie* case of obviousness. Specifically, the Examiner has alleged that obviousness can be shown because Page et al. used the expression “inborn error of metabolism” and teaches “the same clinical presentations” as those observed in patients with mitochondrial disorders.

The Applicant respectfully disagrees. As the Examiner correctly understood previously, it is not enough to use Page et al. alone for making a valid obviousness rejection (see, the Office Action mailed September 13, 2005, page 3, lines 6-8 of the last full paragraph through page 4). The Examiner further quite correctly observed in the same Office Action that the “**combined** teachings of prior art” (i.e., a combination of the teachings of Page et al. and von Borstel) would have provided motivation to administer uridine to treat various specified disorders (see, the Office Action mailed September 13, 2005, page 5, lines 3-6, emphasis added).

Thus, according to the Examiner herself, it is necessary to use von Borstel for making this rejection. Now the Examiner makes the rejection without using von Borstel. Clearly, there is a contradiction between the reasoning set forth in the Office Action mailed September 13, 2005 and that set forth in the present Office Action.

Turning to the present amendment, the Applicant respectfully points out that the limitation “ataxia” has been deleted from each of claims 67 and 91. Accordingly, each of claims 67 and 91 now recites the treatment of

“mitochondrial renal tubular acidosis,

multiple mitochondrial deletion syndrome,
Leigh syndrome, lactic acidemia,
3-hydroxybutyric acidemia, encephalomyopathy,
1+proteinuria, pyruvate dehydrogenase deficiency,
complex I deficiency, complex IV deficiency,
aminoaciduria, hydroxyprolinuria, and
MARIAHS syndrome.”

The Applicants respectfully submits that Page et al. neither disclose nor suggest the treatment of any of these disorders. What Page et al. do disclose is the treatment of various developmental conditions (see, abstract). The conditions themselves are not identified except their manifestations. These manifestations are discussed in terms of clinical presentations and fall into such broad categories as behavioral, speech, neurological, immunological, and other clinical presentation (see, Table 1, page 11602, straddling the left-side column and the right-side column). For example, the conditions are manifested as seizures, ataxia, an awkward gait, mildly impaired motor control, hyperactivity, distractability, deliriousness, an abnormal social interaction and the like (see, e.g., page 11601, left hand column, fourth full paragraph).

However, Page et al. do not provide any disclosure or any suggestion linking any of these manifestations to any specific disease or disorder recited in claims 67 and 91. One skilled in the art would know that the same or similar outward manifestation may characterize various diseases, not just one disease. For example, just because Page et al. provide some guidance with respect to the treatment of some conditions clinically presented as hyperactivity, does not mean that such guidance can be applied to the treatment of a person suffering from a disease recited in claims 67 and 91. Therefore, it is respectfully submitted that one having ordinary skill in the art will not be motivated to use the methods discussed in page et al. and to modify them so as to make them applicable to the treatments recited in claims 67 and 91.

In view of the foregoing, it is respectfully submitted that each of claims 67 and 91 is patentably distinguishable over Page et al. in view of von Borstel. Each of claims 70,

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73, 75-81, and 84-90 depends, directly or indirectly, on claim 67 or on claim 91, and is allowable for at least the same reason. It is also submitted that the rejection of claim 93 does not apply, because claim 93 was previously canceled and is no longer pending. Reconsideration and withdrawal of the rejection are respectfully requested.

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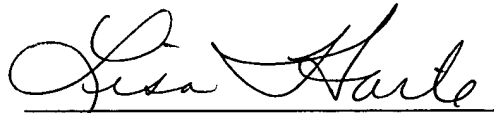
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CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Enclosed is Check No. 582555 in the amount of \$60.00 for the one-month Petition for Extension of Time fee. No other fee is deemed necessary with the filing of this paper. However, if any other fee is required, authorization is hereby given to the Commissioner to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,



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Date: July 7, 2006

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